The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte C. ALEXANDER TURNER JR., MICHAEL C. NEHLS, GLENN FRIEDRICH, BRIAN ZAMBROWICZ, and ARTHUR T. SANDS

Appeal No. 2004-1732
Application No. 09/714,882

MAILED
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U.S. PATENT AND TRADEMARK OFFICE
BOARD OF PATENT APPEALS
AND INTERFERENCES

ON BRIEF

Before WILLIAM F. SMITH, SCHEINER, and GRIMES, Administrative Patent Judges.

GRIMES, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 1-8, all of the claims in the application. Claims 1 and 2 are representative and read as follows:

1. An isolated nucleic acid molecule comprising the nucleotide sequence shown in SEQ ID NO: 1.

2. An isolated nucleic acid molecule comprising a nucleotide sequence that encodes the amino acid sequence shown in SEQ ID NO: 2.

The examiner relies on the following references:

Tischer et al. 5,194,596 Mar. 16, 1993

Massague, "The TGF-β Family of Growth and Differentiation Factors," Cell, Vol. 49, pp. 437-438 (1987)

Pilbeam et al., "Comparison of the Effects of Various Lengths of Synthetic Human Parathyroid Hormone-Related Peptide (hPTHrP) of Malignancy on Bone Resorption and Formation in Organ Culture," Bone, Vol. 14, pp. 717-720 (1993)

Vukicevic et al., "Induction of nephrogenic mesenchyme by osteogenic protein 1 (bone morphogenetic protein 7)," Proc. Natl. Acad. Sci. USA, Vol. 93, pp. 9021-9026 (1996)

Benjamin et al., "A plasticity window for blood vessel remodelling is defined by pericyte coverage of the preformed endothelial network and is regulated by PDGF-B and VEGF," Development, Vol. 125, pp. 1591-1598 (1998)

Biunno et al., "SEL1L, the human homolog of C. elegans sel-1: refined physical mapping, gene structure and identification of polymorphic markers," Human Genetics, Vol. 106, pp. 227-235 (2000)

Yan et al., "Two-Amino Acid Molecular Switch in an Epithelial Morphogen That Regulates Binding to Two Distinct Receptors," Science, Vol. 290, pp. 523-527 (2000)

Baron et al., "Multiple levels of Notch signal regulation (Review)," Molecular Membrane Biology, Vol. 19, pp. 27-38 (2002)

Portin, "General outlines of the molecular genetics of the Notch signalling pathway in Drosophila melanogaster: a review," Hereditas, Vol. 136, pp. 89-96 (2002)

Baron, "An overview of the Notch signalling pathway," Seminars in Cell & Developmental Biology, Vol. 14, pp. 113-119 (2003)

Claims 1-8 stand rejected under 35 U.S.C. §§ 101 and 112, first paragraph, as lacking patentable utility.

We affirm.

Background

The specification discloses nucleic acid sequences that "encode proteins/open reading frames (ORFs) of 689, 688, 590, 418, [and] 499 . . . amino acids in length (see SEQ ID NOS: 2, 4, 6, 8, [and] 10 . . ., respectively)." Page 2.[1] The encoded proteins, generically referred to in the specification as novel human proteins, or NHPs, are said to "share structural similarity with animal Notch ligands, and particularly SEL-1." Id.

"SEL-1 proteins are negative regulators of Notch family receptors. Notch receptors and their associated signaling pathways have been associated with development, apoptosis, neuron growth and maintenance. Genetic alterations in Notch receptors and their ligands have been associated with multiple human processes and disorders such as diabetes, cancer (inter alia, pancreatic cancer and insulinomas), stroke, Alzheimer's and other neurodegenerative diseases, cholesterol and fat metabolism (HMG CoA reductase degradation), blood pressure abnormalities, [c]oronary artery disease and immunity (Donoviel and Bernstein, WO 99/27088, incorporated by reference in its entirety)." Pages 1-2.

The specification does not disclose what role the putative Notch ligands play in any physiological process, but contemplates "processes for identifying compounds that modulate, i.e., act as agonists or antagonists, of NHP expression and/or NHP activity that utilize purified preparations of the described NHPs and/or NHP product, or cells expressing the same. Such compounds can be used as therapeutic agents for the

[1] The examiner characterizes the disclosed polypeptides as "splice variants." Examiner's Answer, page 4. The term "splice variants" implies that all of the disclosed polypeptides are encoded by the same gene and arise through variations in the process of transcription. While the specification does not refer to the different polypeptides as splice variants, the examiner's characterization seems accurate, since SEQ ID NOs 2, 4, 6, 8, and 10 share at least the first 418 amino acids.

treatment of a wide variety of symptoms associated with biological disorders, including, but not limited to, diabetes, heart disease and cancer." Pages 2-3.

The specification also discloses that "suitably labeled NHP nucleotide probes may be used to screen a human genomic library using appropriately stringent conditions or PCR. The identification and characterization of human genomic clones is helpful for identifying polymorphisms . . . , determining the genomic structure of a given locus/allele, and designing diagnostic tests." Page 8.

The specification discloses that "[t]he NHP proteins or peptides, NHP fusion proteins, NHP nucleotide sequences, host cell expression systems, antibodies, antagonists, agonists and genetically engineered cells and animals can be used for screening for drugs . . . effective in the treatment of the symptomatic or phenotypic manifestations of perturbing the normal function of NHP in the body." Page 12. Or "the NHP products can be used as therapeutics. For example, soluble derivatives such as NHP peptides/domains corresponding [to] the NHPs, . . . NHP antibodies . . ., antagonists or agonists . . . can be used to directly treat diseases or disorders." Pages 12-13. In addition, the specification discloses that "[n]ucleotide constructs encoding functional NHPs, mutant NHPs, as well as antisense and ribozyme molecules can also be used in 'gene therapy' approaches for the modulation of NHP expression." Page 13.

The NHP protein is disclosed to have "a variety of uses. These uses include, but are not limited to, the generation of antibodies, as reagents in diagnostic assays, for the identification of other cellular gene products related to a NHP, [and] as reagents in assays for screening for compounds that can be [used?] as pharmaceutical reagents

useful in the therapeutic treatment of mental, biological, or medical disorders and disease." Page 14.

The specification discloses that NHP-binding antibodies "may be used, for example, in the detection of NHP in a biological sample and may, therefore, be utilized as part of a diagnostic or prognostic technique whereby patients may be tested for abnormal amounts of NHP. . . . Such antibodies may additionally be used as a method for the inhibition of abnormal NHP activity. Thus, such antibodies may, therefore, be utilized as part of treatment methods." Pages 23-24.

Discussion

The examiner rejected all of the claims as lacking a disclosed utility sufficient to satisfy 35 U.S.C. § 101.[2] The examiner bears the initial burden of showing that a claimed invention lacks patentable utility. See In re Brana, 51 F.3d 1560, 1566, 34 USPQ2d 1436, 1441 (Fed. Cir. 1995) ("Only after the PTO provides evidence showing that one of ordinary skill in the art would reasonably doubt the asserted utility does the burden shift to the applicant to provide rebuttal evidence sufficient to convince such a person of the invention's asserted utility.").

The seminal decision interpreting the utility requirement of § 101 is Brenner v. Manson, 383 U.S. 519, 148 USPQ 689 (1966). At issue in Brenner was a claim to "a chemical process which yields an already known product whose utility—other than as a possible object of scientific inquiry—ha[d] not yet been evidenced." Id. at 529, 148 USPQ at 693. The Patent Office had rejected the claimed process for lack of utility, on

[2] The examiner also rejected all of the claims under 35 U.S.C. § 112, first paragraph, for lack of enablement, but that rejection is merely as a corollary of the finding of lack of utility. See the Examiner's

the basis that the product produced by the claimed process had not been shown to be useful. See id. at 521-22, 148 USPQ at 690. On appeal, the Court of Customs and Patent Appeals reversed, on the basis that "where a claimed process produces a known product it is not necessary to show utility for the product." Id. at 522, 148 USPQ at 691.

The Brenner Court noted that although § 101 requires that an invention be "useful," that "simple, everyday word can be pregnant with ambiguity when applied to the facts of life." Id. at 529, 148 USPQ at 693. Thus,

> [it] is not remarkable that differences arise as to how the test of usefulness is to be applied to chemical processes. Even if we knew precisely what Congress meant in 1790 when it devised the "new and useful" phraseology and in subsequent re-enactments of the test, we should have difficulty in applying it in the context of contemporary chemistry, where research is as comprehensive as man's grasp and where little or nothing is wholly beyond the pale of "utility"—if that word is given its broadest reach.

Id. at 530, 148 USPQ at 694.[3]

The Court, finding "no specific assistance in the legislative materials underlying § 101," based its analysis on "the general intent of Congress, the purposes of the patent system, and the implications of a decision one way or the other." Id. at 532, 148 USPQ at 695. The Court concluded that "[t]he basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. Unless and until a process is refined and developed to this point—where specific benefit exists in currently available form—

Answer, page 6, second full paragraph. Therefore, our conclusion with respect to the § 101 issue also applies to this § 112 issue.

[3] The invention at issue in Brenner was a process, but the Court expressly noted that its holding "would apply equally to the patenting of the product produced by the process." Id. at 535, 148 USPQ at 695-96.

there is insufficient justification for permitting an applicant to engross what may prove to be a broad field." Id. at 534-35, 148 USPQ at 695.

The Court considered and rejected the applicant's argument that attenuating the requirement of utility "would encourage inventors of new processes to publicize the event for the benefit of the entire scientific community, thus widening the search for uses and increasing the fund of scientific knowledge." The Court noted that, while there is value to encouraging disclosure, "a more compelling consideration is that a process patent in the chemical field, which has not been developed and pointed to the degree of specific utility, creates a monopoly of knowledge which should be granted only if clearly commanded by the statute. Until the process claim has been reduced to production of a product shown to be useful, the metes and bounds of that monopoly are not capable of precise delineation. It may engross a vast, unknown, and perhaps unknowable area. Such a patent may confer power to block off whole areas of scientific development." Id. at 534, 148 USPQ at 695.

The Court took pains to note that it did not "mean to disparage the importance of contributions to the fund of scientific information short of the invention of something 'useful,'" and that it was not "blind to the prospect that what now seems without 'use' may tomorrow command the grateful attention of the public." Id. at 535-36, 148 USPQ at 696. Those considerations did not sway the Court, however, because "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion." Id.

Subsequent decisions of the CCPA and the Court of Appeals for the Federal Circuit have added further layers of judicial gloss to the meaning of § 101's utility

requirement. The first opinion of the CCPA applying Brenner was In re Kirk, 376 F.2d 936, 153 USPQ 48 (CCPA 1967). The invention claimed in Kirk was a set of steroid derivatives said to have valuable biological properties and to be of value "in the furtherance of steroidal research and in the application of steroidal materials to veterinary or medical practice." Id. at 938, 153 USPQ at 50. The claims had been rejected for lack of utility. In response, the applicants submitted an affidavit which purportedly "show[ed] that one skilled in the art would be able to determine the biological uses of the claimed compounds by routine tests." Id. at 939, 153 USPQ at 51.

The court held that "nebulous expressions [like] 'biological activity' or 'biological properties'" did not adequately convey how to use the claimed compounds. Id. at 941, 153 USPQ at 52. Nor did the applicants' affidavit help their case: "the sum and substance of the affidavit appear[ed] to be that one of ordinary skill in the art would know 'how to use' the compounds to find out in the first instance whether the compounds are—or are not—in fact useful or possess useful properties, and to ascertain what those properties are." Id. at 942, 153 USPQ at 53.

The Kirk court held that an earlier CCPA decision, holding that a chemical compound meets the requirements of § 101 if it is useful to chemists doing research on steroids, had effectively been overruled by Brenner. "There can be no doubt that the insubstantial, superficial nature of vague, general disclosures or arguments of 'useful in research' or 'useful as building blocks of value to the researcher' was recognized, and clearly rejected, by the Supreme Court" in Brenner. See Kirk, 376 F.2d at 945, 153 USPQ at 55.

More recently, in In re Ziegler, 992 F.2d 1197, 26 USPQ2d 1600 (Fed. Cir. 1993), the Federal Circuit considered the degree of specificity required to show utility for a claim to polypropylene. The U.S. application on appeal in Ziegler claimed priority to a German application filed in 1954. "In the German application, Ziegler disclosed only that solid granules of polypropylene could be pressed into a flexible film with a characteristic infrared spectrum and that the polypropylene was 'plastic-like.'" Id. at 1203, 26 USPQ2d at 1605. "Ziegler did not assert any practical use for the polypropylene or its film, and Ziegler did not disclose any characteristics of the polypropylene or its film that demonstrated its utility." Id. The court held that the German application did not satisfy the requirements of § 101 and therefore could not be relied on to overcome a rejection based on an intervening reference. See id., 26 USPQ2d at 1606. "[At] best, Ziegler was on the way to discovering a practical utility for polypropylene at the time of the filing of the German application; but in that application Ziegler had not yet gotten there." Id., 26 USPQ2d at 1605.

On the other hand, the CCPA reversed a rejection for lack of utility in In re Jolles, 628 F.2d 1322, 206 USPQ 885 (CCPA 1980). The applicant in Jolles claimed pharmaceutical compositions that were disclosed to be useful in treating acute myeloblastic leukemia. See id. at 1323, 206 USPQ at 886. The active ingredients in the compositions were closely related to daunorubicin and doxorubicin, both of which were "well recognized in the art as valuable for use in cancer chemotherapy." Id., 206 USPQ at 887. The applicant also submitted declaratory evidence showing that eight of the claimed compositions were effective in treating tumors in a mouse model, and one was effective in treating humans. See id. at 1323-24, 206 USPQ at 887-88. The court

noted that the data derived from the mouse model were "relevant to the treatment of humans and [were] not to be disregarded," id. at 1327, 206 USPQ at 890, and held that the evidence was sufficient to support the asserted therapeutic utility. See id. at 1327-28, 206 USPQ at 891.

The Federal Circuit held in Cross v. Iizuka, 753 F.2d 1040, 224 USPQ 739 (Fed. Cir. 1985), that in vivo testing (as in Jolles) was not necessarily required to show utility in the pharmaceutical context. The Cross court stated that "[it] is axiomatic that an invention cannot be considered 'useful,' in the sense that a patent can be granted on it, unless substantial or practical utility for the invention has been discovered and disclosed where such utility would not be obvious." Id. at 1044, 224 USPQ at 742 (citing Brenner v. Manson). The court "perceive[d] no insurmountable difficulty, under appropriate circumstances, in finding that the first link in the screening chain, in vitro testing, may establish a practical utility for the compound in question." Id. at 1051, 224 USPQ at 748. Successful in vitro testing could provide an immediate benefit to the public, by "marshal[ling] resources and direct[ing] the expenditure of effort to further in vivo testing of the most potent compounds . . ., analogous to the benefit provided by the showing of an in vivo utility." Id. On the facts of that case – successful in vitro testing supplemented by similar in vitro and in vivo activities of structurally similar compounds – the court held that in vitro activity was sufficient to meet the requirements of § 101. See id.

The Federal Circuit confirmed in In re Brana, 51 F.3d 1560, 34 USPQ2d 1436 (Fed. Cir. 1995), that human testing is not necessary to establish utility for a method of treatment. The invention claimed in Brana was a group of compounds disclosed to

have antitumor activity. See id. at 1562, 34 USPQ2d at 1437-38. The claimed compounds were disclosed to have higher antitumor activity than related compounds known to have antitumor activity, and the applicants provided declaratory evidence of in vivo activity against tumors in a mouse model. See id., 34 USPQ2d at 1438. The court held that these data were sufficient to satisfy § 101; usefulness in patent law does not require that the invention be ready to be administered to humans. See id. at 1567, 34 USPQ2d at 1442.

Several lessons can be drawn from Brenner and its progeny. First, § 101's requirement that an invention be "useful" is not to be given its broadest reach, such that little or nothing of a chemical nature would be found to lack utility. See Brenner, 383 U.S. at 530, 148 USPQ at 694. Thus, not every "use" that can be asserted will be sufficient to satisfy § 101. For example, the steroid compound at issue in Brenner was useful as a possible object of scientific inquiry, and the polypropylene claimed in Ziegler was useful for pressing into a flexible film, yet both lacked sufficient utility to satisfy § 101. See Brenner, 383 U.S. at 529, 148 USPQ at 696; Ziegler, 992 F.2d at 1203, 26 USPQ2d at 1605.

Rather than setting a de minimis standard, § 101 requires a utility that is "substantial", i.e., one that provides a specific benefit in currently available form. Brenner, 383 U.S. at 534-35, 148 USPQ at 695. This standard has been found to be met by pharmaceutical compositions shown to be useful in mouse models and in humans for treating acute myeloblastic leukemia (Jolles, 628 F.2d at 1327-28, 206 USPQ at 891); by evidence showing successful in vitro testing supplemented by similar in vitro and in vivo activities of structurally similar compounds (Cross, 753 F.2d at 1051,

224 USPQ at 748); and by evidence showing in vivo antitumor activity in mice, combined with a disclosure that the claimed compounds had higher antitumor activity than a related compound known to have antitumor activity (Brana, 51 F.3d at 1567, 34 USPQ2d at 1442).

By contrast, Brenner's standard has been interpreted to mean that "vague, general disclosures or arguments of 'useful in research' or 'useful as building blocks of value to the researcher'" would not satisfy § 101. See Kirk, 376 F.2d at 945, 153 USPQ at 55 (interpreting Brenner). Likewise, a disclosure of a "plastic-like" polypropylene capable of being pressed into a flexible film was held to show that the applicant was "at best . . . on the way to discovering a practical utility for polypropylene at the time of the filing," but not yet there. Ziegler, 992 F.2d at 1203, 26 USPQ2d at 1605.

In this case, the examiner noted that the specification asserts several utilities, but concluded that none of them satisfies § 101:

> The instant application . . . state[s] that the nucleic acids and proteins can be used in methods such as screening assays to identify receptors . . ., use of the nucleic acids to identify mutant alleles, . . . or asses[s] gene expression patterns, for example.
>
> However, none of these uses are considered to be specific or substantial utilities. . . . Methods such as [those disclosed] are considered general methods applicable to any nucleic acid and/or protein, and are not considered specific.
>
> . . .
>
> [T]he assertion that the nucleic acids[ ]and[/]or proteins of the instant invention can be used in the diagnosis or treatment of diseases . . . is based on the assumption that the protein is a ligand in the Notch family, which as a family are involved in myriad biological pathways and activities.
>
> . . .

> . . . The SEL1 protein . . . does not have a specific known function, and is being investigated further to determine what its function and activities are. The skilled artisan would not be able to predict the activities or function of the NHP protein based on 46% similarity to the SEL1 protein, because the SEL1 protein also has no known activity.

Examiner's Answer, pages 4-6.

The examiner concluded that

> [t]he instant claims are drawn to a polynucleotide encoding a protein which has undetermined function or biological significance, and the use of a protein to discover its receptor or properties does not constitute a specific substantial utility. All of the biological activities of a protein need not be known to obtain a patent, but there must be some specific and substantial activity or function known.

Id., page 7.

Appellants argue that

> a sequence that is 99.8% identi[cal] over the 506 amino acid overlap to a described sequence is present in the leading scientific repository for biological sequence data (GenBank), and has been annotated by third party scientists wholly unaffiliated with Appellants as a Novel Protein similar to Sel1L. . . . SEL1L is a well established Notch ligand. . . . As such, the scientific evidence of identity at both the amino acid and nucleic acid levels clearly establishes that those of skill in the art would recognize the sequences of the present invention as a human Notch Ligand, a class of proteins with well known function.

Appeal Brief, pages 4-5.

Appellants cite two post-filing references that are alleged to support the specification's statement (page 14, lines 12-23) that "[b]ecause of the diverse activities that have been associated with Notch signaling pathways, Notch receptors, and their associated ligands and antagonists have been subject to intense scientific scrutiny." Id., page 5. Finally (with respect to this argument), Appellants point to the specification's citation of Donoviel (PCT application WO 99/27088) that "[g]enetic alterations in Notch

receptors and their ligands have been associated with" various disorders; Appellants conclude that "[t]he utility of Notch proteins and ligands are therefore clearly well-known to those of skill in the art." Id.

We do not agree that the characterization of the claimed nucleic acids as encoding a Notch receptor ligand is sufficient to establish their utility. The specification admits that "diverse activities . . . have been associated with Notch signaling pathways," yet the specification provides no information regarding what activities or pathways involve the polypeptides encoded by the instantly claimed nucleic acids.

Although the specification cites Donoviel as disclosing that Notch receptors and ligands have been associated with a variety of disorders, we do not agree that the reference supports that assertion. The relevant disclosure in Donoviel is limited to a human gene designated Sel-1L (for "Sel-1 like"). Donoviel teaches that Sel-1L

> maps to the same chromosomal interval as PS1 [presenilin-1, see page 1, line 11], making it a candidate for an Alzheimer's Disease associated gene. Sel-1L may also play a role in the etiology of other neurodegenerative diseases such as Parkinson's Disease. Sel-1L is expressed in the floor plate of the neural tube during specification of the dopaminergic neurons via contact-mediated induction by the floor plate. Dopaminergic neurons are absent in Parkinson's Disease patients. Sel-1L also maps very close to a microsatellite marker (D14s67) that has been linked to a locus affecting Insulin Dependent Diabetes Mellitus (IDDML). The expression of Sel-1L in neural and pancreatic tissues also suggests that the gene may have a role in pancreatic cancer. Individuals exhibiting AD pathology in post-mortem examinations have been found to have a prevalence of pancreatic cancer over any other type of cancer and over the incidence of this tumor type in non-AD individuals. . . . Sel-1L may also have a role in fat and cholesterol metabolism which is a contributing factor in AD, and conditions such as coronary heart disease.

Page 2, lines 18-29. Based on these properties, apparently, Donoviel discloses that Sel-1L can be used in treating various conditions. See page 4, lines 33-39.

Importantly, Donoviel does not disclose that Sel-1L is a Notch ligand, nor does it suggest that any of the putative therapeutic utilities of Sel-1L are based on sequence similarity to Sel-1. Rather, as the above-quoted passage shows, Donoviel's assertions of therapeutic utility are based on the chromosomal location of Sel-1L (the same chromosomal interval as presenilin-1 and close to a genetic marker linked with diabetes) and the expression of Sel-1L in "the floor plate of the neural tube during specification of the dopaminergic neurons." The association with a putative Alzheimer's disease-associated gene, in turn, led Donoviel to conclude that Sel-1L may be involved in cancer (especially pancreatic cancer) and fat and cholesterol metabolism.

In the present case, Appellants have pointed to no evidence in the record to show that the claimed nucleic acids map near the locus of presenilin-1 or any other Alzheimer's disease-associated gene, or that they map near a diabetes-associated marker, or that they are expressed in the floor plate of the neural tube during specification of dopaminergic neurons. Thus, the claimed nucleic acids do not share the properties that seem to have led to Donoviel's disclosures of therapeutic utility.

In addition, Appellants have not shown that the amino acid sequences of the polypeptides encoded by the claimed nucleic acids would have led those skilled in the art to expect them to have the properties of Donoviel's Sel-1L. The specification discloses only that the encoded polypeptides have some unspecified degree of "structural similarity with animal Notch ligands, and particularly SEL-1." Page 1. As discussed above, however, the record does not support Appellants' position that this disclosure would have suggested a specific biological function, or any other basis for

patentable utility, to a person skilled in the art at the time the application was filed.[4] In the terms used by the Brenner Court, such a characterization does not provide a specific utility in currently available form. We therefore reject Appellants' argument that § 101 is satisfied by the "structural similarity" of the encoded proteins to proteins that are Notch receptor ligands.

Appellants also argue that the claimed polynucleotides are useful because of the disclosed polymorphism at position 1177 of SEQ ID NO:1: "the skilled artisan would readily recognize and easily believe that the presently described polymorphic markers [sic] could be useful in forensic analysis. The fact that forensic biologists use polymorphic markers such as those described by Appellants every day provides more tha[n] ample support for the assertion that forensic biologists would also be able to use the specific polymorphic markers [sic] described by Appellants in the same fashion." Appeal Brief, pages 10-11.

This argument is not persuasive because, among other things, it has no support in the specification or in the evidence of record. The specification discloses the presence of a polymorphism in SEQ ID NO:1 (page 14) but discloses no utilities based on detection of the polymorphism. The specification does not disclose that the polymorphism is a useful marker for either forensic analysis or paternity testing.

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[4] Whether a claimed invention is supported by a disclosure of utility sufficient to satisfy 35 U.S.C. § 101 is determined as of the filing date of the application. See In re Brana, 51 F.3d 1560, 1566 n.19, 34 USPQ2d 1436, 1441 n.19 (Fed. Cir. 1995) ("Enablement, or utility, is determined as of the application filing date."). Therefore, we have not considered the post-filing references cited by the examiner and Appellants as disclosing the biological activities of Sel-1 and other Notch receptor ligands. Those post-filing references include the GenBank record submitted as Exhibit A to the Appeal Brief and the references by Portin, Biunno et al., Baron et al., and Baron.

Appellants cite the specification at page 8, line 12, and page 14, line 30, as disclosing "the use of the present sequences in such diagnostic assays . . . as those associated with identification of paternity and forensic analysis, among others." Appeal Brief, page 10.

We do not agree that those passages support the present argument. The sentence that includes page 8, line 12, of the specification reads as follows:

> For example, sequences derived from regions adjacent to the intron/exon boundaries of the human gene can be used to design primers for use in amplification assays to detect mutations within the exons, introns, splice sites (e.g., splice acceptor and/or donor sites), etc., that can be used in diagnostics and pharmacogenomics.

The sentence that includes page 14, line 30, reads:

> These uses [of NHP polypeptides] include, but are not limited to, the generation of antibodies, as reagents in diagnostic assays, for the identification of cellular gene products related to a NHP, as reagents in assays for screening for compounds that can be as pharmaceutical reagents in the therapeutic treatment of mental, biological, or medical disorders and disease.

Neither of the cited passages refers to polymorphisms, forensic analysis, or paternity testing. Thus, the cited passages do not support the utility asserted in the Appeal Brief.

Appellants have cited no other evidence of record to show that such uses were well-established as of the effective filing date of the present application (November 17, 1999). Nor have Appellants provided any evidence to show that those skilled in the art would have found the specific polymorphism present in SEQ ID NO:1 – without analysis of its degree of variability in the human population and without associating it with any other genetic marker – to be useful as argued. Thus, the polymorphism-based utilities

asserted in the Appeal Brief lacks evidentiary support and cannot be relied on to overcome the rejection.

In addition to the polymorphism-based argument, Appellants also argue that the claimed nucleic acids are useful in "gene chip" methods of tracking gene expression, and that "knowledge of the exact function or role of the presently claimed sequence is not required to track expression patterns using a DNA chip. Appeal Brief, page 8. See also pages 8-9:

> Such "DNA chips" clearly have utility, as evidenced by hundreds of issued U.S. Patents. . . . Clearly, compositions that enhance the utility of such DNA gene chips, such as the presently claimed sequences encoding a testis specific Notch ligand, must in themselves be useful.

Appellants argue that, in addition to their use in "DNA chips", the claimed sequences are also useful "in determining the genomic structure of the corresponding human chromosome . . ., for example mapping the protein encoding regions." Id., page 12. More particularly, Appellants argue that

> [t]he presently claimed polynucleotide sequence [sic] provides biologically validated empirical data (e.g., showing which sequences are transcribed, spliced, and polyadenylated) that specifically defines that portion of the corresponding genomic locus that actually encodes exon sequence.

Id. Appellants argue that "the described sequences are useful for functionally defining exon splice-junctions," and that "the practical scientific value of expressed, spliced, and polyadenylated mRNA sequences is readily apparent to those skilled in the relevant biological and biochemical arts." Id., page 13.

We are not persuaded by Appellants' argument. We find that the asserted uses of the claimed polynucleotides—as a component of a DNA chip for monitoring gene expression, as a marker for a given chromosomal locus, or for defining the exon splice-

junctions of a gene—do not satisfy the utility requirement of § 101. Such uses do not provide a specific benefit in currently available form.

For example, with regard to the asserted "DNA chip" utility, we accept for argument's sake that a person skilled in the art could attach one of the claimed polynucleotides (or a part of it) to a solid substrate, in combination with other polynucleotides, to form a DNA chip, and that such a DNA chip could be used to monitor changes in expression of the corresponding gene. However, the specification provides no guidance to allow a skilled artisan to use data relating to the expression of the gene comprising SEQ ID NO:1 in any practical way. The specification provides no guidance regarding what the SEQ ID NO:1-specific information derived from a DNA chip would mean.

For example, assume that a fragment of SEQ ID NO:1 was attached to a DNA chip and the researcher observed that expression of the corresponding gene was increased when a cell was treated with a particular agent. The specification provides no basis on which a skilled worker would be able to determine what, if anything, that result means. Perhaps a change in expression of the gene would mean different things, depending on other factors, but again the specification provides no hint what other factors might be important. Would it depend on what agent is used, what cell type is used, the behavior of other genes (if so, which genes and what behavior is significant), or the degree of increase? Because the specification provides no information about the activity of the protein encoded by SEQ ID NO:1, it provides no guidance as to how to interpret the results of a DNA chip-based gene expression assay based on the claimed polynucleotides.

The same problem afflicts Appellants' assertions that the claimed polynucleotides can be used to map a particular chromosomal locus or to define the exon splice-junctions of the genomic gene: the specification provides no meaningful guidance regarding how to use such information in any practical way. What would it mean, for example, if SEQ ID NO:1 hybridizes to a specific part of human chromosome 4, or if SEQ ID NO:1 can be used to show that the chromosomal gene has an exon splice junction between nucleotides 103 and 104? The specification provides no guidance on how such information would allow those skilled in the art to use the claimed polynucleotides in a specific, substantial way. By contrast, if the specification disclosed, for example, that SEQ ID NO:1 hybridized adjacent to a chromosomal locus associated with a known disease (e.g., a locus susceptible to a cancer-causing translocation), the sequence would have an apparent utility in disease diagnosis. However, without disclosure of a specific use for the resulting data, using the claimed sequences for mapping or determining exon splice-junctions amounts to research on the claimed polynucleotides themselves.

In effect, Appellants' position is that the claimed polynucleotides are useful because those of skill in the art could experiment with them and figure out for themselves what any observed experimental results might mean. We do not agree that such a disclosure provides a "specific benefit in currently available form." Rather, the instant case seems analogous to Brenner. In Brenner, the applicant claimed a method of making a compound but disclosed no utility for the compound. 383 U.S. at 529, 148 USPQ at 693. The Court held that a process lacks utility if it produces a product that lacks utility. Id. at 534, 148 USPQ at 695. Here, Appellants claim a product asserted to

be useful in a method of generating gene-expression or gene-mapping data, but the specification does not disclose how to interpret those data. Just as the process claimed in Brenner lacked utility because the specification did not disclose how to use the end-product, the product claims here lack utility, based on their use in, e.g., DNA chips, because the specification does not disclose how to use the SEQ ID NO:1-specific gene expression data generated by a DNA chip.

Appellants argue that the claimed polynucleotides could potentially be part of a DNA chip; since DNA chips have utility, compounds that "enhance the utility of such DNA chips, such as the presently claimed nucleotide sequence, must in themselves be useful." Appeal Brief, pages 8-9. We disagree.

Assuming arguendo that a generic DNA chip—one comprising a collection of uncharacterized or semi-characterized gene fragments—would provide a useful tool for, e.g., drug discovery, it does not follow that each one of the polynucleotides represented in the DNA chip individually has patentable utility. Although each polynucleotide in the DNA chip contributes to the data generated by the DNA chip overall, the contribution of a single polynucleotide—its data point—is only a tiny contribution to the overall picture.

The Brenner Court held that § 101 sets more than a de minimis standard for utility. Therefore, the patentable utility of a DNA chip, for example, does not necessarily mean that every one of the components of the DNA chip also has patentable utility. A patentable utility divided by a thousand does not necessarily equal a thousand patentable utilities. Each claimed invention must be shown to meet § 101's utility requirement in order to be patentable; it must provide a specific benefit in currently

available form. Providing a single data point among thousands, even if the thousands of data points collectively are useful, does not meet this standard.

The Supreme Court noted that the patent system contemplates a basic quid pro quo: in exchange for the legal right to exclude others from his invention for a period of time, an inventor discloses his invention to the public. See Brenner, 383 U.S. at 534, 148 USPQ at 695. The Brenner Court held that the grant of patent rights to an applicant is justified only by disclosure of an invention with substantial utility – a specific benefit in currently available form. Until the invention has been refined and developed to this point, the Court held, the applicant has not met his side of the bargain, and has not provided a disclosure that justifies granting him the right to exclude others. See id.

Thus, the basic quid pro quo of the patent system is the grant of a valuable legal right in exchange for a meaningful disclosure of the claimed invention. In this case, the generic utilities disclosed for the claimed products do not entitle Appellants to the legal right they claim to exclude others from using those products.

We note that this application is one of several on appeal that share the same assignee.[5] In each of these cases, regardless of the specific facts of the case, the appellants have asserted the same DNA chip, gene-mapping, and exon splice junction arguments. It would therefore appear that Appellants view these potential uses as utilities that can be asserted for any cDNA they isolate, regardless of how little is known about it, which (they hope) will nonetheless serve as a basis for patent protection and secure for Appellants any value that might become apparent in the future, after they or

[5] Such applications include 09/460,594 (Appeal No. 2003-1528), 09/804,969 (2003-1794); 09/802,116 (2003-2017); 09/822,807 (2003-2028); and 09/564,557 (2004-0343).

others have further characterized the claimed products. This is precisely the type of result that the Brenner Court sought to avoid by requiring disclosure of a substantial utility to satisfy § 101. See 148 U.S. at 535-36, 148 USPQ at 696: [The Court was not] "blind to the prospect that what now seems without 'use' may tomorrow command the grateful attention of the public. But a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion." Id.

The polynucleotides of the instant claims may indeed prove to be useful (and valuable), after the in vivo role of the encoded protein is discovered. The work required to confer value on the claimed products, however, remains to be done. The instant specification's disclosure does not justify a grant of patent rights. See Brenner, 383 U.S. at 534, 148 USPQ at 695: "[A] process patent in the chemical field, which has not been developed and pointed to the degree of specific utility, creates a monopoly of knowledge which should be granted only if clearly commanded by the statute. Until the process claim has been reduced to production of a product shown to be useful, the metes and bounds of that monopoly are not capable of precise delineation. It may engross a vast, unknown, and perhaps unknowable area. Such a patent may confer power to block off whole areas of scientific development." We consider the Brenner Court's concern about the "power to block off whole areas of scientific development" to be equally applicable here.

Finally, adopting the per se rule that Appellants seek—that any expressed human gene has utility because it can be used in a DNA chip—would mean that almost any naturally occurring nucleic acid would be patentable. Appellants' reasoning does not depend on the biological function of the protein encoded by the claimed nucleic

acids, and so would apparently apply to any expressed human gene, as well as fragments of them (see, e.g., the specification at page 8, lines 24-32).

Nor can the rationale be confined to expressed human genes. We can take judicial notice of the fact that other organisms are of interest for many different reasons, such that gene expression assays could conceivably be used in their research. For example, some organisms are of interest to researchers because they have been historically well-studied (e.g., yeast and Arabidopsis). Others are of interest because they are used as animal models (e.g., mice and chimpanzees), because they are commercially valuable (e.g., pigs and tomatoes), because they are pests (e.g., ragweed and corn borers), or because they are pathogens (e.g., Candida and various bacteria). Under Appellants' proposed rule, hybridizable fragment of any gene of any of these organisms—and probably most other organisms—would be found to have patentable utility because it could be attached to a chip and used in "research" to see what happens to expression of that gene under various conditions.

Appellants' reasoning would also vitiate the enablement requirement, since "[t]he enablement requirement is met if the description enables any mode of making and using the invention." Johns Hopkins Univ. v. CellPro Inc., 152 F.3d 1342, 1361, 47 USPQ2d 1705, 1714 (Fed. Cir. 1998) (quoting Engel Indus., Inc. v. Lockformer Co., 946 F.2d 1528, 1533, 20 USPQ2d 1300, 1304 (Fed. Cir. 1991)). If we were to agree with Appellants that any expressed gene and any hybridizable fragment thereof is useful in a DNA chip, then we would also have to hold that the specification has taught those skilled in the art one mode of using the invention. Thus, Appellants' rule of per se utility would also require a corresponding rule of per se enablement.

Under Appellants' rule, then, any polynucleotide from an expressed gene would be patentable if it was adequately described in the specification and was not disclosed or suggested in the prior art. This standard, however, is not the one set by Congress, which requires that a patentable invention also be useful and fully enabled, nor is it the standard that has been consistently applied by the courts.

In addition, the flood of DNA patents that would result from adoption of Appellants' rule could doom the potential contribution of microarrays to biological research. Appellants argue that "[g]iven the widespread utility of such 'gene chip' methods using public domain gene sequence information, there can be little doubt that the use of the presently described novel sequences would have great utility in such DNA chip applications." Appeal Brief, page 8. See also page 9: "[T]here is an entire industry established based on the use of gene sequences or fragments thereof in a gene chip format."

The practical effect of Appellants' utility standard, however, would be that making a microarray with 1000 genes represented on it would require investigating each of the DNA sequences (and subsequences) on the gene chip to ensure that it was not the subject of someone else's patent. For each of the DNAs that was the subject of someone else's patent claim, a license would have to be negotiated – potentially thousands of such negotiations for the finished product. These transaction costs would have to be incurred for each new product that an aspiring gene chip manufacturer wished to market. The industry gridlock likely to result has been termed a "tragedy of the anticommons:"

> By conferring monopolies in discoveries, patents necessarily increase prices and restrict use—a cost society pays to motivate invention and disclosure. The tragedy of the anticommons refers to the more complex obstacles that arise when a user needs access to multiple patented inputs to create a single useful product. Each upstream patent allows its owner to set up another tollbooth on the road to product development, adding to the cost and slowing the pace of downstream biomedical innovation.

Heller, page 698.[6]

The Supreme Court has warned against allowing too many "tollbooths" on the road to innovation:

> Patents . . . are meant to encourage invention by rewarding the inventor with the right, limited to a term of years fixed by the patent, to exclude others from the use of his invention. . . . But in rewarding useful invention, the "rights and welfare of the community must be fairly dealt with and effectually guarded." Kendall v. Winsor, 21 How. 322, 329 (1859). . . . To begin with, a genuine "invention" or "discovery" must be demonstrated "lest in the constant demand for new appliances the heavy hand of tribute be laid on each slight technological advance in an art."

Sears, Roebuck & Co. v. Stiffel Co., 376 U.S. 225, 230, 140 USPQ 524, 527 (1964).

[6] Heller et al., "Can patents deter innovation? The anticommons in biomedical research," Science, Vol. 280, pp. 698-701 (1998). Accessible online at www.sciencemag.org/cgi/content/full/280/5364/698.

Summary

The basic quid pro quo of the patent system requires disclosure of an invention having substantial utility. Appellants' disclosure in this case does not provide a specific benefit in currently available form, and therefore lacks the substantial utility required by 35 U.S.C. § 101. We therefore affirm the rejections for lack of utility.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

AFFIRMED

William F. Smith
Administrative Patent Judge

Toni R. Scheiner
Administrative Patent Judge

Eric Grimes
Administrative Patent Judge

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Lexicon Genetics Incorporated
8800 Technology Forest Place
The Woodlands TX 77381-1160